

## AMENDMENTS TO THE CLAIMS

**1. (Currently Amended)** A cobalamin derivative of formula (I):

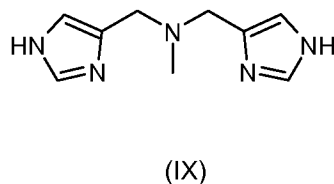
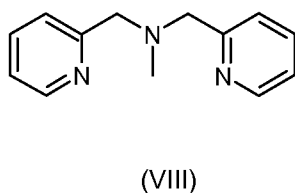
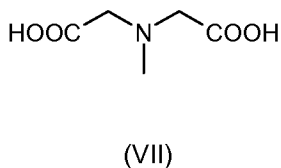
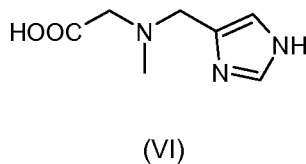
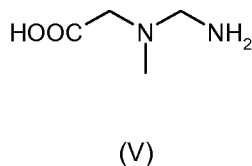
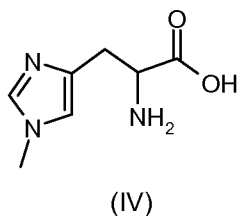
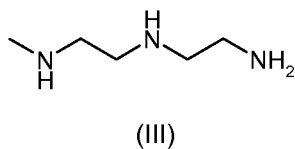
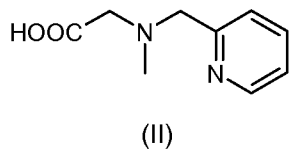


wherein:

- (ii)  $R^c$ ,  $R^d$ , and  $R^e$ , and  $R^R$  are an antibiotic or antiproliferative therapeutic agent, ~~each connected through a linker Z, or hydrogen; and  $R^R$  is an antibiotic or antiproliferative therapeutic agent connected through a linker Z, or hydrogen;~~

- (iv) X is cyano, methyl, hydroxy, aquo or a 5'-deoxyadenosyl group; and

(v) the central cobalt (Co) atom is optionally in the form of a radioactive isotope; and wherein the spacer-chelator group consists of an aliphatic chain of 2 to 4 carbon atoms carrying a chelator selected from the chelators of formulae (II) to (IX):



wherein carboxyl groups in formulae (II) to (IX) may be present as esters; and said cobalamin derivative:

- (a) has no binding affinity or less than 20% binding affinity to transcobalamin II when compared to the binding affinity of non-modified cobalamin in a binding test, and
- (b) retains activity as a vitamin B12 substitute.

**2. (Previously Presented)** The cobalamin derivative according to claim 1 retaining more than 2% of the activity as a vitamin B12 substitute in a growth assay.

**3. (Original)** The cobalamin derivative according to claim 1

(a) having less than 10% of binding affinity to transcobalamin II when compared to the binding affinity of non-modified cobalamin in a binding test, and

(b) retaining more than 10% of the activity as a vitamin B12 substitute in a growth assay.

**4. (Original)** The cobalamin derivative according to claim 1

(a) having less than 5% of binding affinity to transcobalamin II when compared to the binding affinity of non-modified cobalamin in a binding test, and

(b) retaining more than 10% of the activity as a vitamin B12 substitute in a growth assay.

**5. (Previously presented)** The cobalamin derivative according to claim 1 carrying a therapeutic and/or diagnostic agent.

**6. (Previously presented)** The cobalamin derivative according to claim 1 carrying a radioactive metal.

**7-10. (Cancelled)**

**11. (Previously presented)** The cobalamin derivative according to claim 6 wherein the radioactive metal is  $^{94m}\text{Tc}$ ,  $^{99m}\text{Tc}$ ,  $^{188}\text{Re}$ ,  $^{186}\text{Re}$ ,  $^{111}\text{In}$ ,  $^{90}\text{Y}$ ,  $^{64}\text{Cu}$ ,  $^{67}\text{Cu}$  or  $^{177}\text{Lu}$ .

**12. (Cancelled)**

**13. (Previously Presented)** The cobalamin derivative according to claim 1 wherein X is cyano.

**14. (Previously Presented)** The cobalamin derivative according to claim 1, wherein the central cobalt atom is the radioisotope  $^{57}\text{Co}$  or  $^{60}\text{Co}$ .

**15. (Previously Presented)** The cobalamin derivative according to claim 1, wherein  $R^b$  is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 2 to 4 carbon atoms, and the chelator is of formula (II), wherein the group COOH is optionally in the form of an ester;  
 $R^c$ ,  $R^d$ ,  $R^e$  and  $R^R$  are hydrogen; and  
X is cyano.

**16. (Previously Presented)** The cobalamin derivative according to claim 15, wherein  $R^b$  is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 4 carbon atoms, and the chelator is of formula (II), wherein the group COOH is in the form of the ethyl ester;  
 $R^c$ ,  $R^d$ ,  $R^e$  and  $R^R$  are hydrogen; and  
X is cyano.

**17. (Previously Presented)** The cobalamin derivative according to claim 1, wherein  $R^d$  is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 3 carbon atoms, and the chelator is of formula (II), wherein the group COOH is optionally in the form of an ester;  
 $R^b$ ,  $R^c$ ,  $R^e$  and  $R^R$  are hydrogen; and  
X is cyano.

**18. (Previously Presented)** The cobalamin derivative according to claim 1, wherein  $R^b$  is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 2 carbon atoms, and the chelator is of formula (III);  
 $R^c$ ,  $R^d$ ,  $R^e$  and  $R^R$  are hydrogen; and  
X is cyano.

**19. (Previously presented)** A pharmaceutical composition comprising a cobalamin derivative according to claim 1.

**20. (Previously Presented)** A method of diagnosis of a neoplastic disease in a mammal comprising

- (a) exposing the mammal suspected of being inflicted by a neoplastic disease or an infection to a period of a vitamin B12 – free diet, and
- (b) subsequently applying a cobalamin derivative according to claim 1 carrying a diagnostic agent.

**21. (Currently Amended)** A method of treatment of a mammal suffering from ~~a neoplastic disease~~ melanoma comprising

- (a) exposing the mammal in need of treatment to a period of a vitamin B12 – free diet, and
- (b) subsequently applying a cobalamin derivative according to claim 1 carrying a therapeutic agent.

**22-25. (Cancelled)**

**26. (Previously presented)** The method of claim 20, wherein the cobalamin is effective in cancer imaging.

**27. (Cancelled)**